=> d ibib abs ind l52

L52 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:286767 HCAPLUS
DOCUMENT NUMBER: 140:292615
TITLE: Concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation
INVENTOR(S): **Kumpe, Gerhardt; Juraschek, Manfred ; Mayer, Natascha; Schulte, Stefan ; Wormsbaecher, Wilfried**
PATENT ASSIGNEE(S): Aventis Behring G.m.b.H., Germany
SOURCE: Eur. Pat. Appl., 14 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1405863	A1	20040407	EP 2003-20148	20030905
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
DE 10246125	A1	20040415	DE 2002-10246125	20021001
US 2004132654	A1	20040708	US 2003-670563	20030926
CA 2443463	AA	20040401	CA 2003-2443463	20030929
JP 2004123744	A2	20040422	JP 2003-339076	20030930
PRIORITY APPLN. INFO.:			DE 2002-10246125 A	20021001

AB The invention concerns a blood product that is a concentrate of blood coagulation factor von Willebrand (vWF) and VIIIc complex; the concentrate is prepared from a fluid that contains the two factors; fractionated precipitation is performed in a way that high mol. weight components of vWF are enriched and a ratio of vWF-Ristocetin-cofactor activity (vWF:RCoF) to vWF-Antigen (vWF:Ag) being greater than 1 is established. Plasma, plasma fractions, cryoppts., and genetically modified cells are the starting materials. For fractionated precipitation amino acids, especially glycine, salts, especially sodium chloride are used. The product or pre-products are sterilized and stabilized with calcium-ion containing agent. The dissolved cryoppt. is treated before the fractionated precipitation: mixing with alumina results the adsorption of entrapped prothrombin complexes; glycine ppts. fibrin. The concentrate is used to treat von Willebrand syndrome and hemophilia A.

IC ICM C07K014-755
ICS A61K038-37; A61P007-04
CC 63-3 (Pharmaceuticals)
ST conc blood coagulation factor VIIIC von Willebrand hemophilia
IT Hemophilia
(A; concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)
IT Adsorption
Blood products
Molecular weight
Sterilization and Disinfection
Von Willebrand's disease
(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)
IT Fibrins
RL: REM (Removal or disposal); PROC (Process)

(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT Amino acids, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT Precipitation (chemical)
(fractionated; concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT Antigens
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(von Willebrand's factor; concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT 7440-70-2, Calcium, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(-containing stabilizing agent; concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT 1344-28-1, Alumina, biological studies 9001-27-8, Blood coagulation factor VIII, complex
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT 9001-26-7, Prothrombin
RL: REM (Removal or disposal); PROC (Process)
(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

IT 56-40-6, Glycine, biological studies 7647-14-5, Sodium chloride, biological studies 109319-16-6, Blood-coagulation factor VIII, von Willebrand's 113189-02-9, Blood coagulation factor VIIIc
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(concentrate of von-Willebrand blood coagulation factor-factor VIIIc complex and method for preparation)

```
=> d his ful

     FILE 'HCAPLUS' ENTERED AT 12:12:05 ON 27 JUL 2005
                E KUMPE GERHARDT/AU
                E KUMPE GERHARDT/AU
L47          20 SEA ABB=ON  ("KUMPE G"/AU OR "KUMPE GERHARD"/AU OR "KUMPE
                GERHARDT"/AU)
                E JURASCHEK MANFRED/AU
L48           2 SEA ABB=ON  ("JURASCHEK M"/AU OR "JURASCHEK MANFRED"/AU)
                E MAYER NATASCHA/AU
L49           6 SEA ABB=ON  ("MAYER N M"/AU OR "MAYER NATALIE"/AU OR "MAYER
                NATASCHA"/AU)
                E SCHULTE STEFAN/AU
L50           9 SEA ABB=ON  "SCHULTE STEFAN"/AU
                E WORMSHABACHER WILFRIED/AU
                E WORMSBACH/AU
L51           9 SEA ABB=ON  ("WORMSBAECHER WILFRIED"/AU OR "WORMSBAECHER
                WINFRIED"/AU)
L52           1 SEA ABB=ON  L47 AND L48 AND L49 AND L50 AND L51
L53             ANALYZE L52 1-1 CT :       10 TERMS

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L54           1 SEA ABB=ON  9001-27-8/RN
L55           1 SEA ABB=ON  109319-16-6/RN
L56           1 SEA ABB=ON  56-40-6/RN
L57           1 SEA ABB=ON  7647-14-5/RN

     FILE 'HCAPLUS' ENTERED AT 13:36:08 ON 27 JUL 2005
L58       10492 SEA ABB=ON  (L54 OR ?FACTOR?(W)VIIIC) OR (L55 OR VON?(W)?WILLEB
                RAND?)
L59          37 SEA ABB=ON  L58 AND ?PRECIPITAT?(4A)?FRACTION?
L60          12 SEA ABB=ON  L59 AND (L56 OR ?GLYCINE?)
L61           6 SEA ABB=ON  L59 AND (L57 OR NACL OR ?SODIUM?(W)?CHLORIDE?)
L62          14 SEA ABB=ON  L60 OR L61
L63           2 SEA ABB=ON  L62 AND (?AMINO?(W)?ACID? OR (?ALKALI? OR ?ALKALINE
                ?)(W)?METAL?)
L64           3 SEA ABB=ON  L59 AND (?AMINO?(W)?ACID? OR ?ALKAL?(W)?METAL?)
L65          15 SEA ABB=ON  L62 OR L63 OR L64
L66           2 SEA ABB=ON  L65 AND (?STABILIZ? OR ?PASTEURIZ?)
L67          15 SEA ABB=ON  L65 OR L66

     FILE 'MEDLINE, BIOSIS, EMBASE, JAPIO, JICST-EPLUS' ENTERED AT 13:49:10 ON
     27 JUL 2005
L68          11 SEA ABB=ON  L67
L69           6 DUP REMOV L68 (5 DUPLICATES REMOVED) 6 cite from above db's

     FILE 'USPATFULL' ENTERED AT 13:53:07 ON 27 JUL 2005
L70         277 SEA ABB=ON  L65 OR L66
L71         241 SEA ABB=ON  L70 AND (PRD<20021001 OR PD<20021001)
L72         154 SEA ABB=ON  L71 AND ((L57 OR NACL OR ?SODIUM?(W)?CHLORIDE?)
                AND (L56 OR ?GLYCINE?))
L73           7 SEA ABB=ON  L72 AND ?FRACTIONAL?(W)(?PRECIPITAT? OR ?CONCENTRAT
                ?)  7 cite from USPATFULL

     FILE 'HCAPLUS' ENTERED AT 14:24:05 ON 27 JUL 2005
L74          14 SEA ABB=ON  L67 AND (PRD<20021001 OR PD<20021001)  14 cite from
                                                                   CA Plus
     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
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provided by InfoChem.

STRUCTURE FILE UPDATES: 26 JUL 2005 HIGHEST RN 857144-48-0
DICTIONARY FILE UPDATES: 26 JUL 2005 HIGHEST RN 857144-48-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

FILE HCAPLUS

FILE COVERS 1907 - 27 Jul 2005 VOL 143 ISS 5
FILE LAST UPDATED: 26 Jul 2005 (20050726/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE MEDLINE
FILE LAST UPDATED: 26 JUL 2005 (20050726/UP). FILE COVERS 1950 TO DATE.

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow promt (=>). See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 July 2005 (20050721/ED)

FILE RELOADED: 19 October 2003.

FILE EMBASE
FILE COVERS 1974 TO 21 Jul 2005 (20050721/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE JAPIO
FILE LAST UPDATED: 4 JUL 2005 <20050704/UP>
FILE COVERS APR 1973 TO MARCH 31, 2005

<<< GRAPHIC IMAGES AVAILABLE >>>

FILE JICST-EPLUS
FILE COVERS 1985 TO 25 JUL 2005 (20050725/ED)

THE JICST-EPLUS FILE HAS BEEN RELOADED TO REFLECT THE 1999 CONTROLLED TERM (/CT) THESAURUS RELOAD.

FILE USPATFULL
FILE COVERS 1971 TO PATENT PUBLICATION DATE: 26 Jul 2005 (20050726/PD)
FILE LAST UPDATED: 26 Jul 2005 (20050726/ED)
HIGHEST GRANTED PATENT NUMBER: US6922846
HIGHEST APPLICATION PUBLICATION NUMBER: US2005160510
CA INDEXING IS CURRENT THROUGH 26 Jul 2005 (20050726/UPCA)
ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 26 Jul 2005 (20050726/PD)
REVISED CLASS FIELDS (/NCL) LAST RELOADED: Jun 2005
USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Jun 2005

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
>>> original, i.e., the earliest published granted patents or <<<
>>> applications. USPAT2 contains full text of the latest US <<<
>>> publications, starting in 2001, for the inventions covered in <<<
>>> USPATFULL. A USPATFULL record contains not only the original <<<
>>> published document but also a list of any subsequent <<<
>>> publications. The publication number, patent kind code, and <<<
>>> publication date for all the US publications for an invention <<<
>>> are displayed in the PI (Patent Information) field of USPATFULL <<<
>>> records and may be searched in standard search fields, e.g., /PN, <<<
>>> /PK, etc. <<<

>>> USPATFULL and USPAT2 can be accessed and searched together <<<
>>> through the new cluster USPATALL. Type FILE USPATALL to <<<
>>> enter this cluster. <<<
>>> <<<
>>> Use USPATALL when searching terms such as patent assignees, <<<
>>> classifications, or claims, that may potentially change from <<<
>>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L55           1 SEA FILE=REGISTRY ABB=ON  109319-16-6/RN
L56           1 SEA FILE=REGISTRY ABB=ON  56-40-6/RN
L57           1 SEA FILE=REGISTRY ABB=ON  7647-14-5/RN
L58       10492 SEA FILE=HCAPLUS ABB=ON  (L54 OR ?FACTOR?(W)VIIIC) OR (L55 OR
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L59          37 SEA FILE=HCAPLUS ABB=ON  L58 AND ?PRECIPITAT?(4A)?FRACTION?
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L62          14 SEA FILE=HCAPLUS ABB=ON  L60 OR L61
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L74          14 SEA FILE=HCAPLUS ABB=ON  L67 AND (PRD<20021001 OR PD<20021001)

=> d ibib abs l74 1-14

L74  ANSWER 1 OF 14  HCAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2001:884943  HCAPLUS
DOCUMENT NUMBER:          136:163110
TITLE:                    A novel human metalloprotease synthesized in the liver
                          and secreted into the blood: possibly, the von
                          Willebrand factor-cleaving protease?
AUTHOR(S):                Soejima, Kenji; Mimura, Noriko; Hirashima, Masaki;
                          Maeda, Hiroaki; Hamamoto, Takayoshi; Nakagaki,
                          Tomohiro; Nozaki, Chikateru
CORPORATE SOURCE:         First Research Department, The Chemo-Sero-Therapeutic
                          Research Institute, Kumamoto, 869-1298, Japan
SOURCE:                   Journal of Biochemistry (Tokyo, Japan) (2001
                          ), 130(4), 475-480
                          CODEN: JOBIAO; ISSN: 0021-924X
PUBLISHER:                Japanese Biochemical Society
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   We identified a novel metalloprotease which could be responsible for
     cleaving the Tyr842-Met843 peptide bond of von
     Willebrand factor (vWF). This metalloprotease was purified from
     Cohn Fraction-I precipitate of human pooled plasma by the
     combination of gel filtration, DEAE chromatog., and preparative PAGE in
     the presence of SDS. The NH2-terminal amino acid
     sequence of the isolated protein was: AAGGILHLELLVAVGPDVFQAHQEDTRRY.
     Based on this sequence, we searched human genomic and EST databases, and
     identified compatible nucleotide sequences. These results suggested that
     this protein is a novel metalloprotease, a member of the family of a
     disintegrin and metalloprotease with thrombospondin type-1 motifs
     (ADAMTS), and its genomic DNA was mapped to human chromosome 9q34.
     Multiple human tissue northern blotting anal. indicated that the mRNA
     encoding this protease spanned approx. 5 kilobases and was uniquely
     expressed in the liver. Furthermore, we determined the cDNA sequence encoding
     this protease, and found that this protease was comprised of a signal
     peptide, a proregion followed by the putative furin cleavage site, a
     reprolysin-type zinc-metalloprotease domain, a disintegrin-like domain, a
     thrombospondin type-1 (TSP1) motif, a cysteine-rich region, a spacer
```

domain, and COOH-terminal TSP1 motif repeats.
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L74 ANSWER 2 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1990:154827 HCAPLUS
DOCUMENT NUMBER: 112:154827
TITLE: DEAE-chromatographic separation of plasma proteins
INVENTOR(S): Burnouf, Thierry; Burnouf, Myriana
PATENT ASSIGNEE(S): Centre Regional de Transfusion Sanguine de Lille, Fr.
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8912065	A1	19891214	WO 1989-FR50	19890208 <--
W: AU, DK, FI, JP, KR, NO, SU, US				
RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
FR 2632309	A1	19891208	FR 1988-7530	19880607 <--
FR 2632309	B1	19900824		
AU 8930682	A1	19900105	AU 1989-30682	19890208 <--
AU 622436	B2	19920409		
EP 359593	A1	19900321	EP 1989-400348	19890208 <--
EP 359593	B1	19950426		
EP 359593	B2	20040107		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
JP 03501974	T2	19910509	JP 1989-502342	19890208 <--
AT 121750	E	19950515	AT 1989-400348	19890208 <--
ES 2070919	T3	19950616	ES 1989-400348	19890208 <--
CA 1340742	A1	19990914	CA 1989-590961	19890214 <--
FI 96210	B	19960215	FI 1990-397	19900125 <--
FI 96210	C	19960527		
NO 9000529	A	19900406	NO 1990-529	19900205 <--
NO 177188	B	19950424		
NO 177188	C	19950802		
DK 9000299	A	19900328	DK 1990-299	19900206 <--
DK 175322	B1	20040823		
SU 1837880	A3	19930830	SU 1990-4743107	19900206 <--
KR 9710923	B1	19970702	KR 1990-70239	19900206 <--
US 5252709	A	19931012	US 1990-460972	19900406 <--
AU 9211383	A1	19920514	AU 1992-11383	19920303 <--
DK 200400872	A5	20040603	DK 2004-872	20040603 <--

PRIORITY APPLN. INFO.:	FR 1988-7530	A	19880607 <--
	WO 1989-FR50	A	19890208 <--
	DK 1990-299	L	19900206 <--

AB A method for separating proteins from human or animal plasma comprises subjecting a solubilized **fraction** of **cryopptd.** plasma to a single step of chromatog. on an anion-exchange resin which has a moderate ionic character and that favors hydrophobic interactions, permitting retention of very large mols. The proteins are eluted by increasing the ion strength of the buffer (e.g., by adding **NaCl**). A high-purity concentrate of factor VIII was obtained using Fractogel TSK-DEAE 650, e.g. for use in the treatment of hemophilia A (no data). In the process of obtaining factor VIII, concentrate of fibrinogen, **von Willebrand**'s factor, and fibronectin were also obtained. These

proteins were further purified by chromatog.

L74 ANSWER 3 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1988:479751 HCAPLUS
DOCUMENT NUMBER: 109:79751
TITLE: Process for the preparation of lyophilized and heat-treated blood coagulation factor VIII
INVENTOR(S): Schwarz, Otto; Linnau, Yendra
PATENT ASSIGNEE(S): Immuno A.-G. fuer Chemisch-Medizinische Produkte, Austria
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 270516	A2	19880608	EP 1987-890237	19871029 <--
EP 270516	A3	19880622		
EP 270516	B1	19910403		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
AT 8602923	A	19900615	AT 1986-2923	19861103 <--
AT 391808	B	19901210		
US 4814435	A	19890321	US 1987-108458	19871015 <--
CA 1297011	A1	19920310	CA 1987-549552	19871019 <--
AT 62133	E	19910415	AT 1987-890237	19871029 <--
ES 2028913	T3	19920716	ES 1987-890237	19871029 <--
DK 8705735	A	19880504	DK 1987-5735	19871102 <--
JP 63132899	A2	19880604	JP 1987-278985	19871102 <--
JP 07030117	B4	19950405		

PRIORITY APPLN. INFO.: AT 1986-2923 A 19861103 <--
EP 1987-890237 A 19871029 <--

AB A process for the preparation of a factor VIII (I)-containing fraction with a specific activity of <2.5 units/mg protein and IgG content of <10 mg/1000 units I is described. In the presence of sulfate group-containing polysaccharides, proteins are precipitated at neutral pH and removed from a I-containing plasma **fraction**, then I is **precipitated** from this by treatment with a protein precipitating agent, such as (NH4)2SO4, **glycine**/(NH4)2SO4, **glycine/NaCl**, Na2SO4, (NH4)2SO4/Na citrate, or **glycine**/citrate. The I-containing precipitate is dissolved and lyophilized and the lyophilizate is heat-treated for virus inactivation. A cryoppt. (150 g) was dissolved in a solution containing 900 mL 3-Na citrate buffer, 90 mg sulfate group-containing polysaccharide (SP 54), 9 units Atheplex, and 27,000 units apotinin and the pH was adjusted to 6.25 at 4°, the protein-containing precipitate was removed and the concentration of **glycine** and (NH4)2SO4 was adjusted to 120 g/L and 85 g/L, resp. The resulting precipitate was dissolved in **NaCl**/citrate buffer and dialyzed, the **glycine** and albumin concns. in the dialyzate were adjusted to 10 mg/L and 2 mg/L, resp. and the solution was lyophilized and heat-treated. The activity of I (moisture content 7.9%) after heat-treatment for 10 h at 60° was 53.6 units/mL, after 100 h at 60° it was 40.0 units/mL, whereas for a non-treated lyophilizate the activity was 54.7 units/mL.

L74 ANSWER 4 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1986:39704 HCAPLUS
DOCUMENT NUMBER: 104:39704

TITLE: High purity antihemophilic factor concentrate
INVENTOR(S): Mitra, Gautam; Ng, Paul K.
PATENT ASSIGNEE(S): Miles Laboratories, Inc. , USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 4543210	A	19850924	US 1984-658081	19841004 <--
CA 1243950	A1	19881101	CA 1985-486007	19850628 <--
JP 61087626	A2	19860506	JP 1985-167835	19850731 <--
JP 06076337	B4	19940928		
EP 176926	A2	19860409	EP 1985-112070	19850924 <--
EP 176926	A3	19871028		
EP 176926	B1	19890628		
R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
AT 44236	E	19890715	AT 1985-112070	19850924 <--
DK 8504507	A	19860405	DK 1985-4507	19851003 <--
DK 163107	B	19920120		

PRIORITY APPLN. INFO.: US 1984-658081 A 19841004 <--
EP 1985-112070 A 19850924 <--

AB High-purity antihemophilic factor, having high sp. activity and low fibrinogen impurities, is prepared from blood plasma or a blood plasma **fraction** by **precipitation** with polyethylene glycol (PEG) plus Al(OH)3, followed by a 2nd precipitation with PEG plus **glycine** and **NaCl.** Thus, 400 g cryoppt. in 4 volume H2O was treated with 64 mL 2% Al(OH)3 and PEG 3350, to obtain 3% PEG in the solution The pH was adjusted to 6.7 with 1M AcOH. The solution was cooled to 9° and centrifuged at 8500 rpm, for 15 min. The supernatant was separated and treated with 148 g PEG 3350. From this solution, the factor VIII was precipitated with 13% **glycine** (240.5 g) and 14% **NaCl** (259 g), at pH 5.7. The precipitate was washed with **glycine/NaCl** buffer at 2°, centrifuged and dissolved in 400 g citrate-**NaCl-glycine** buffer (pH 7.2-7.4) to give a high-purity antihemophilic factor solution

L74 ANSWER 5 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1985:119614 HCAPLUS
DOCUMENT NUMBER: 102:119614
TITLE: Antihemophilic factor VIII concentrate
INVENTOR(S): Rasmussen, Mirella Ezban; Nordfang, Ole
PATENT ASSIGNEE(S): Nordisk Insulinlaboratorium, Den.
SOURCE: PCT Int. Appl., 21 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 8403628	A1	19840927	WO 1984-DK19	19840320 <--
W: AU, DK, FI, JP, NO, US				
RW: AT, BE, CH, DE, FR, GB, LU, NL, SE				

DK 8305494	A	19840922	DK 1983-5494	19831201 <--
DK 157170	B	19891120		
DK 157170	C	19960812		
DK 8400646	A	19841110	DK 1984-646	19840214 <--
AU 8428101	A1	19841009	AU 1984-28101	19840320 <--
EP 148843	A1	19850724	EP 1984-901337	19840320 <--
EP 148843	B1	19900124		
R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE				
AT 49706	E	19900215	AT 1984-901337	19840320 <--
US 4650858	A	19870317	US 1984-673753	19841030 <--
FI 8404557	A	19841120	FI 1984-4557	19841120 <--
FI 80382	B	19900228		
FI 80382	C	19900611		
NO 8404610	A	19841120	NO 1984-4610	19841120 <--
NO 169875	B	19920511		
NO 169875	C	19920819		

PRIORITY APPLN. INFO.:	DK 1983-1274	A	19830321 <--
	DK 1984-646	A	19830509 <--
	DK 1983-5494	A	19831201 <--
	EP 1984-901337	A	19840320 <--
	WO 1984-DK19	A	19840320 <--

AB Pure blood-coagulation Factor VIII (I) [**9001-27-8**] with high solubility and activity, free of other proteins, especially Igs, is obtained by fractionating a cryoppt. with PEG [25322-68-3] such that at least 80% of the fibrinogen is 1st precipitated and then precipitating in a subsequent step with more PEG in the presence of a salting-in agent such as an **amino acid** or carbohydrate. The high purity of I permits it to be redissolved in a very small volume of aqueous injection medium in a concentration of 45-500 units/mL. PEG with a mol. weight of 3000 is preferred, its concentration in the 1st precipitate being 2-6% and in the 2nd precipitate 6-20% by weight The pH in the 1st precipitate is 6.0-8.5 and in the 2nd precipitate 5.0-8.5. The temperature in both steps is 18-22°. Cryoppt. from human blood plasma, other Factor VIII-containing blood fractions, and blood fractions from other animal species can be used. Thus, a cryoppt. from 600 mL human blood plasma was dissolved in 28 mL citrate/glucose buffer, freed of prothrombin by adsorption on Al2O3, then 4% PEG was added, the pH adjusted to 6.4 with 0.5M HCl, the mixture incubated for 30 min at room temperature, the precipitated protein removed, lysine-HCl [657-27-2] 0.55 mol/mL was added, followed by addition of 8% PEG, the pH adjusted to 6.3 with 0.1M NaOH, the mixture incubated for 45 min at room temperature, centrifuged, and the precipitate redissolved in citrate/glucose-**NaCl**, pH 7.8. The redissolved precipitate has a specific activity of 12 units I/mg protein, and yield of 20%.

L74 ANSWER 6 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1981:546586 HCAPLUS
DOCUMENT NUMBER:	95:146586
TITLE:	The potential of heparin as an agent for precipitation of plasma fibronectin (CIg) and certain components of the plasma factor VIII complex
AUTHOR(S):	Mosesson, Michael W.; Amrani, David L.
CORPORATE SOURCE:	Downstate Med. Cent., State Univ. New York, Brooklyn, NY, 11203, USA
SOURCE:	Developments in Biochemistry (**1981**),

12(Chem. Biol. Heparin), 105-11
CODEN: DEBIDR; ISSN: 0165-1714
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A heparin (I) concentration of 0.15-0.25 mg/mL was optimal for precipitation of plasma fibronectin and coagulation factor VIII components, and subsequent I removal was accomplished by TEAE-cellulose. Approx. 85% of the plasma fibronectin was precipitated at 0.2 mg I/mL. Less than 5% of the factor VIII procoagulant activity was precipitated by I; however it could be recovered in the supernatant by cryopptn., cold EtOH, and **glycine.** Willebrand ristocetin cofactor was precipitated by I (≥95% of the activity), and Willebrand antigen was distributed approx. equally between the **ppt** . and supernatant **fractions.**

L74 ANSWER 7 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1980:90181 HCAPLUS
DOCUMENT NUMBER: 92:90181
TITLE: Preparation and properties of bovine factor VIII (antihemophilic factor)
AUTHOR(S): Vehar, Gordon A.; Davie, Earl W.
CORPORATE SOURCE: Dep. Biochem., Univ. Washington, Seattle, WA, 98195, USA
SOURCE: Biochemistry (**1980**), 19(3), 401-10
CODEN: BICHAW; ISSN: 0006-2960
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Factor VIII was purified approx. 300,000-fold from bovine plasma by ammonium sulfate **fractionation, glycine pptn** ., DEAE-Sephadex column chromatog., sulfate-Sepharose column chromatog., Sephadex G-200 gel filtration, and factor X-Sepharose column chromatog. The highly purified preparation migrated as a triplet on Na dodecyl sulfate-urea-polyacrylamide gel electrophoresis with apparent mol. wts. of 93,000, 88,000, and 85,000. The coagulant activity of the purified prepns. was inhibited by antibodies raised in rabbits against either the purified factor VIII protein or a preparation of factor VIII/**von Willebrand** factor. Antibodies to the purified protein also inhibited the coagulant activity of factor VIII/**von Willebrand** factor prepns. The purified factor VIII contained no platelet-aggregating activity, as measured in human platelet-rich plasma. The purified preparation of factor VIII was required for the activation of factor X in the presence of factor IXa, Ca, and phospholipid. It was activated about 30-fold by thrombin or factor Xa plus Ca and phospholipid, and each of these reactions was accompanied by a change in the Na dodecyl sulfate-urea-polyacrylamide gel electrophoresis pattern of the protein. Factor VIII was rapidly inactivated by bovine-activated protein C in a reaction requiring Ca and phospholipid. This reaction was also associated with a change in the Na dodecyl sulfate-urea-polyacrylamide gel electrophoresis pattern of the highly purified protein. These expts. involving 3 highly specific serine proteases support the conclusion that the triplet observed on polyacrylamide gels is factor VIII.

L74 ANSWER 8 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1975:520820 HCAPLUS
DOCUMENT NUMBER: 83:120820
TITLE: **Stabilization** of AHF [antihemophilic factor]
PATENT ASSIGNEE(S): Baxter Laboratories, Inc., USA
SOURCE: Brit., 5 pp.

CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
GB 1372515	A	19741030	GB 1973-23187	19730515 <--
US 3803115	A	19740409	US 1972-254148	19720517 <--
ZA 7303138	A	19740327	ZA 1973-3138	19730509 <--
JP 49056695	A2	19740601	JP 1973-54039	19730514 <--
JP 59006845	B4	19840215		
BE 799525	A1	19730831	BE 1973-131099	19730515 <--
NL 7306806	A	19731120	NL 1973-6806	19730516 <--
FR 2184898	A1	19731228	FR 1973-17649	19730516 <--
CA 1007986	A1	19770405	CA 1973-171527	19730516 <--
NO 142381	B	19800505	NO 1973-2027	19730516 <--
NO 142381	C	19800813		
CH 630804	A	19820715	CH 1973-7001	19730516 <--
AU 7355849	A1	19741121	AU 1973-55849	19730517 <--
AT 7304335	A	19750415	AT 1973-4335	19730517 <--
ES 414823	A1	19760201	ES 1973-414823	19730517 <--
DK 136016	B	19770801	DK 1973-2745	19730517 <--
SE 430020	B	19831017	SE 1973-7018	19730517 <--
SE 430020	C	19840126		
US 29698	E	19780711	US 1976-674270	19760406 <--

PRIORITY APPLN. INFO.: US 1972-254148 A 19720517 <--

AB AHF was obtained in improved yield from blood plasma by addition of 0.01-10 units heparin [9005-49-6] per ml to a cryoppt. concentrate This concentrate was precipitated with 3-4% polyethylene glycol 4000, the resultant supernatant precipitated with .apprx.10% polyethylene glycol 4000, and this **precipitate fractionated** with 1.8M **glycine.** Heparin increased the final AHF yield by 25-35% over the nonheparinized procedure.

L74 ANSWER 9 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:562646 HCAPLUS
DOCUMENT NUMBER: 77:162646
TITLE: Fractionation of plama using **glycine** and polyethylene glycol
INVENTOR(S): Fekete, Lajos F.; Shanbrom, Edward
PATENT ASSIGNEE(S): Baxter Laboratories, Inc.
SOURCE: U.S., 7 pp. Continuation-in-part of U.S. 3,560,475 (CA 74;96677c).
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 3682881	A	19720808	US 1970-77491	19701002 <--
GB 1303408	A	19730117	GB 1971-76017	19711004 <--
CA 962591	A1	19750211	CA 1971-124332	19711004 <--

PRIORITY APPLN. INFO.: US 1970-77491 A 19701002 <--

AB Concns. of antihemophilic factor A and prothrombin complex are prepared from citrated blood plasma by an initial fractionation with **glycine**

followed by multiple fractionations of the antihemophilic factor-containing precipitate and the prothrombin complex-containing supernate with polyethylene glycol; the **precipitate** is given an addnl. **fractionation** with **glycine** and the supernate is given an intermediate adsorption with tribasic Ca phosphate. A fractionation flow chart is included.

L74 ANSWER 10 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1972:22762 HCAPLUS
DOCUMENT NUMBER: 76:22762
TITLE: Large-scale preparation of factor VIII-concentrate from frozen cryoethanol precipitate
AUTHOR(S): Wickerhauser, M.
CORPORATE SOURCE: Blood Res. Lab., Am. Natl. Red Cross, Washington, DC, USA
SOURCE: Thrombosis et Diathesis Haemorrhagica, Supplementum (**1971**), No. 43, 165-73
CODEN: TDHSAF; ISSN: 0375-9997
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The original polyethylene glycol (PEG) procedure was modified for the large-scale recovery of antihemophilic factor (AHF) from frozen cryoethanol precipitate (cryo). Frozen cryo, obtained by combined cryopptn. and 3% EtOH precipitation of freshly frozen plasma prior to large-scale Cohn fractionation, was extracted with Tris buffer, 60 min at 30°, starting with 4.6 kg cryo. The extract was treated with Al(OH)3 gel. The precipitate was separated by means of a continuous flow centrifuge, and discarded. Na citrate was added to the solution, followed by citric acid to pH 6.05. PEG 4000 was added to a final concentration of 4.8% to **precipitate** the fibrinogen **fraction.** The AHF was then precipitated by precipitation at 11% PEG. Excess PEG was removed by washing with buffer containing PEG, Tris, and Na citrate at pH 6.0. The precipitate was reconstituted in buffer containing Tris, Na citrate, and **NaCl** (0.075M) at pH 7.0. The resulting solution was sterilized by filtration. The filtered concentrate was frozen and lyophilized. Filtrable factor VIII concs. were obtained, 80-100-fold purified, with a yield of 5 AHF units/g cryo.

L74 ANSWER 11 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1970:82961 HCAPLUS
DOCUMENT NUMBER: 72:82961
TITLE: Stable, high-potency human antihemophilic factor (AHF)
PATENT ASSIGNEE(S): Baxter Laboratories, Inc.
SOURCE: Brit., 6 pp.
CODEN: BRXXAA
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE	
GB 1178958		19700128			<--
DE 1767285			DE		
FR 1589414			FR		
US 3631018		19710000	US		<--
PRIORITY APPLN. INFO.:			US	19670501	<--

AB A stable AHF of high potency is prepared by the fractionation of a cryoppt. concentrate of human or animal AHF. Cryoppt. refers to the precipitate which is obtained from freezing of the blood plasma at ≤4° and separating the precipitate formed from the supernatant. **Fractionation** was accomplished by **precipitating** the redissolved **fraction** of the AHF concentrate with a 1.3-1.8M aqueous solution of **glycine**, followed by the recovery and redissolution of the precipitate Recovery was accomplished either by centrifugation or filtration and redissoln. was achieved by warming and agitating in a citrated saline solution An alternative method was two successive pptns. with polyethylene glycol (PEG) (mol. weight 200-20,000, but PEG 4000 was preferred). The first pptn was accomplished with 3-4% PEG by weight of the cryoppt. of AHF followed by recovery of the resulting supernate and subsequent precipitation with 10% glycol by weight of the supernate followed by recovery of the resulting precipitate The PEG precipitation step could also be employed in combination with the **glycine** precipitation step. The fractionated cryoppt. concentrate of AHF was treated by chromatographic purification by successive absorption, and elution from an Ecteola cellulose resin, either by column or batch techniques. The concentrate purified by this method was suitable for administration either by i.m. or i.v. administration. The Ecteola purified concentrate was free of fibrinogen by the addition of thrombin and by immunoelectrophoresis.

L74 ANSWER 12 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1968:112707 HCAPLUS
DOCUMENT NUMBER: 68:112707
TITLE: Chromatographic purification of fibrinogen
AUTHOR(S): Finlayson, John S.
CORPORATE SOURCE: Nat. Insts. of Health, Bethesda, MD, USA
SOURCE: Fibrinogen (**1968**), 39-59
CODEN: 19YKAU
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Fibrinogen (I) is apparently chromatographically heterogeneous. I was prepared by previously described methods and also by a "phosphate" and a "**glycine**" method (details not given). I was heterogeneous regardless of its source or the method of preparation More than 30 sep. forms of I were obtained from a single sample of plasma, in which clottable protein (II) was essentially constant The distribution of II in the elution patterns (in column chromatog.) from the plasma in patients with macroglobulinemia, hemophilia A, **von Willebrand**'s disease, or dysfibrinogenemia did not differ from that in normal I, although in dysfibrinogenemia 1 peak was eluted later than usual. In human I, the 2 major peaks separable by DEAE-cellulose chromatog. were present in I isolated from umbilical cord blood and in the high-solubility I not **precipitated** in Cohn **fraction** I. Chromatographic properties of I from different species of animals are considered. 60 references.

L74 ANSWER 13 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1967:408602 HCAPLUS
DOCUMENT NUMBER: 67:8602
TITLE: A semiautomatic one-stage factor VIII assay with a commercially prepared standard
AUTHOR(S): Simone, Joseph V.; Vanderheiden, Jane; Abildgaard, Charles F.

CORPORATE SOURCE: Coll. of Med., Univ. of Illinois, Chicago, IL, USA
SOURCE: Journal of Laboratory and Clinical Medicine (**1967**), 69(4), 706-12
CODEN: JLCMAK; ISSN: 0022-2143
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A one-stage factor VIII assay with a semiautomatic clot-timer and a com. standard plasma is described. Compared to existing methods, this assay is tech. simpler, more quickly performed, and less subject to human error. The 95% confidence limits of individual assays, which is a superior estimate of uncertainty for parallel-line bioassays, averaged 80-127% of the observed result even at very high or very low levels. The mean factor VIII level for 60 normal subjects was 101% with a range of 58-200%. Serial factor VIII assays in 6 normal subjects revealed wide fluctuations over the 60-day study period. This method also allows assay of factor VIII in cryoppt. and **glycine-precipitate fractions** of plasma.

L74 ANSWER 14 OF 14 HCAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1959:29433 HCAPLUS
DOCUMENT NUMBER: 53:29433
ORIGINAL REFERENCE NO.: 53:5369f-g
TITLE: Purification of antihemophilic globulin. I. Stability of antihemophilic globulin activity in fraction I-O and a method for its partial separation from fibrinogen
AUTHOR(S): Blomback, Margareta
SOURCE: Arkiv foer Kemi (**1958**), 12, 387-96
CODEN: ARKEAD; ISSN: 0365-6128
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable

AB When fraction I-O (purified Cohn fraction I) is extracted with **glycine** at pH 6.8 instead of pH 6.0 as originally devised, a good yield of antihemophilic globulin activity (AHA) is obtained. Rapid freezing of fraction I-O or fraction I-1-A at about -30° (in citrate solution at pH 6.3) gave the most constant AHG values. Slow freezing at about -15° produces great loss of activity; at -5° almost all activity is lost. A method is presented for separation of AHA from the fibrinogen in **fraction** I-O by **precipitation** at ionic strength 0.1 in the presence of **glycine**, with about 80% yield and good purification. The fibrinogen can be recovered from the supernatant by precipitation with a yield of about 70% of the amount present in fraction I-O and a coagulability of about 92%. 48 references.

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=> d que stat l69
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L55             1 SEA FILE=REGISTRY ABB=ON  109319-16-6/RN
L56             1 SEA FILE=REGISTRY ABB=ON  56-40-6/RN
L57             1 SEA FILE=REGISTRY ABB=ON  7647-14-5/RN
L58         10492 SEA FILE=HCAPLUS ABB=ON  (L54 OR ?FACTOR?(W)VIIIC) OR (L55 OR
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L59            37 SEA FILE=HCAPLUS ABB=ON  L58 AND ?PRECIPITAT?(4A)?FRACTION?
L60            12 SEA FILE=HCAPLUS ABB=ON  L59 AND (L56 OR ?GLYCINE?)
L61             6 SEA FILE=HCAPLUS ABB=ON  L59 AND (L57 OR NACL OR ?SODIUM?(W)?CH
                  LORIDE?)
L62            14 SEA FILE=HCAPLUS ABB=ON  L60 OR L61
L63             2 SEA FILE=HCAPLUS ABB=ON  L62 AND (?AMINO?(W)?ACID? OR (?ALKALI?
                   OR ?ALKALINE?)(W)?METAL?)
L64             3 SEA FILE=HCAPLUS ABB=ON  L59 AND (?AMINO?(W)?ACID? OR ?ALKAL?(W
                  )?METAL?)
L65            15 SEA FILE=HCAPLUS ABB=ON  L62 OR L63 OR L64
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L67            15 SEA FILE=HCAPLUS ABB=ON  L65 OR L66
L68            11 SEA L67
L69             6 DUP REMOV L68 (5 DUPLICATES REMOVED)

=> d ibib abs l69 1-6

L69  ANSWER 1 OF 6     MEDLINE on STN                    DUPLICATE 1
ACCESSION NUMBER:   2001528350     MEDLINE
DOCUMENT NUMBER:    PubMed ID: 11574066
TITLE:              A novel human metalloprotease synthesized in the liver and
                    secreted into the blood: possibly, the von
                    Willebrand factor-cleaving protease?.
COMMENT:            Erratum in: J Biochem (Tokyo) 2001 Nov;130(5):719
AUTHOR:             Soejima K; Mimura N; Hirashima M; Maeda H; Hamamoto T;
                    Nakagaki T; Nozaki C
CORPORATE SOURCE:   First Research Departmen, The Chemo-Sero-Therapeutic
                    Research Institute, Kumamoto 869-1298, Japan..
                    soejima@kaketsuken.or.jp
SOURCE:             Journal of biochemistry, (2001 Oct) 130 (4) 475-80.
                    Journal code: 0376600. ISSN: 0021-924X.
PUB. COUNTRY:       Japan
DOCUMENT TYPE:      Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:           English
FILE SEGMENT:       Priority Journals
OTHER SOURCE:       GENBANK-AB069698
ENTRY MONTH:        200201
ENTRY DATE:         Entered STN: 20011001
                    Last Updated on STN: 20020226
                    Entered Medline: 20020130
AB  We identified a novel metalloprotease, which could be responsible for
    cleaving the Tyr842-Met843 peptide bond of von
    Willebrand factor (vWF). This metalloprotease was purified from
    Cohn Fraction-I precipitate of human pooled plasma by
    the combination of gel filtration, DEAE chromatography, and preparative
    polyacrylamide gel electrophoresis in the presence of SDS. The
    NH2-terminal amino acid sequence of the isolated
    protein was: AAGGILHLELLVAVGPDVFQAHQEDTRRY. Based on this sequence, we
    searched human genomic and EST databases, and identified compatible
    nucleotide sequences. These results suggested that this protein is a
    novel metalloprotease, a member of the family of a disintegrin and
    metalloprotease with thrombospondin type-1 motifs (ADAMTS), and its
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genomic DNA was mapped to human chromosome 9q34. Multiple human tissue northern blotting analysis indicated that the mRNA encoding this protease spanned approximately 5 kilobases and was uniquely expressed in the liver. Furthermore, we determined the cDNA sequence encoding this protease, and found that this protease was comprised of a signal peptide, a proregion followed by the putative furin cleavage site, a reprolysin-type zinc-metalloprotease domain, a disintegrin-like domain, a thrombospondin type-1 (TSP1) motif, a cysteine-rich region, a spacer domain, and COOH-terminal TSP1 motif repeats.

L69 ANSWER 2 OF 6 MEDLINE on STN
ACCESSION NUMBER: 84250234 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6330903
TITLE: Activated protein C inhibitor.
AUTHOR: Suzuki K
SOURCE: Seminars in thrombosis and hemostasis, (1984 Apr) 10 (2) 154-61.
Journal code: 0431155. ISSN: 0094-6176.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198407
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19990129
Entered Medline: 19840727

L69 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 80130523 MEDLINE
DOCUMENT NUMBER: PubMed ID: 7356933
TITLE: Preparation and properties of bovine factor VIII (antihemophilic factor).
AUTHOR: Vehar G A; Davie E W
SOURCE: Biochemistry, (1980 Feb 5) 19 (3) 401-10.
Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198005
ENTRY DATE: Entered STN: 19900315
Last Updated on STN: 19900315
Entered Medline: 19800523

AB Factor VIII has been purified approximately 300000-fold from bovine plasma by ammonium sulfate **fractionation, glycine precipitation**, DEAE-Sephadex column chromatography, sulfate--Sepharose column chromatography, Sephadex G-200 gel filtration, and factor X--Sepharose column chromatography. The highly purified preparation migrated as a triplet on sodium dodecyl sulfate/urea--polyacrylamide gel electrophoresis with apparent molecular weights of 93000, 88000, and 85000. The coagulant activity of the purified preparations was inhibited by antibodies raised in rabbits against either the purified factor VIII protein or a preparation of factor VIII/ **von Willebrand** factor. Antibodies to the purified protein also inhibited the coagulant activity of factor VIII/**von Willebrand** factor preparations. The purified factor VIII contained no platelet-aggregating activity, as measured in human platelet-rich plasma. The purified preparation of factor VIII was required for the activation of factor X in the presence of factor IXa,

calcium, and phospholipid. It was activated about 30-fold by thrombin or factor Xa plus calcium and phospholipid, and each of these reactions was accompanied by a change in the sodium dodecyl sulfate/urea--polyacrylamide gel electrophoresis pattern of the protein. Factor VIII was rapidly inactivated by bovine-activated protein C in a reaction requiring calcium and phospholipid. This reaction was also associated with a change in the sodium dodecyl sulfate/urea--polyacrylamide gel electrophoresis pattern of the highly purified protein. These experiments involving three highly specific serine proteases support the conclusion that the triplet observed on polyacrylamide gels is factor VIII.

L69 ANSWER 4 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 74025944 EMBASE
DOCUMENT NUMBER: 1974025944
TITLE: Isolation and characterization of human factor VIII (antihemophilic factor).
AUTHOR: Legaz M.E.; Schmer G.; Counts R.B.; Davie E.W.
CORPORATE SOURCE: Dept. Biochem., Univ. Washington Sch. Med., Seattle, Wash. 98195, United States
SOURCE: Journal of Biological Chemistry, (1973) Vol. 248, No. 11, pp. 3946-3955.
CODEN: JBCHA3
DOCUMENT TYPE: Journal
FILE SEGMENT: 029 Clinical Biochemistry
025 Hematology
LANGUAGE: English
AB Factor VIII (antihemophilic factor) has been purified approximately 500 fold from the **cryoprecipitate fraction** of human plasma. The isolation procedure involves adsorption of contaminants with Al(OH)3, column chromatography on tricalcium citrate cellulose, precipitation with concanavalin A, and an agarose gel filtration step. The final product is homogeneous when examined by zone electrophoresis, sedimentation equilibrium, and immunoelectrophoresis. The molecular weight determined by sedimentation equilibrium is 1.12 x 106 ± 98,000. After reduction of the protein with 2 mercaptoethanol or dithiothreitol, subunits are formed which migrate as one band in polyacrylamide gel electrophoresis and zone electrophoresis. The subunits are heterogeneous however, in the ultracentrifuge, apparently due to substantial aggregation. The smallest species which could be detected has a molecular weight of 1.05 x 105 ± 5,000. The molecular weight of the subunit determined by sodium dodecyl sulfate (SDS) gel electrophoresis was 240,000. The latter value may be high, however, due to the fact that human Factor VIII contains approximately 6% carbohydrate (hexose, hexosamine, and neuraminic acid) and the molecular weights of glycoproteins determined by SDS gel electrophoresis tend to be high. Antibodies prepared in rabbits against human Factor VIII inhibit both human and bovine Factor VIII activity. Antibodies to the highly purified human Factor VIII also form a precipitin line in immunoelectrophoresis experiments with the **cryoprecipitate fraction** prepared from hemophilic plasma, indicating that an abnormal Factor VIII molecule is present in the plasma of individuals with classic hemophilia. Other general properties of human Factor VIII, including its **amino acid** composition, thrombin modification, and turnover in hemophilic dogs, are also reported.

L69 ANSWER 5 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 74155784 EMBASE

DOCUMENT NUMBER: 1974155784
TITLE: **Von Willebrand**'s disease in Sweden.
AUTHOR: Silwer J.
CORPORATE SOURCE: Coagulat. Lab., Univ. Lund, Sweden
SOURCE: Acta Paediatrica Scandinavica, (1973) Vol. 62, No. 238 sup., pp. 159p..
CODEN: APSVAM
DOCUMENT TYPE: Journal
FILE SEGMENT: 037 Drug Literature Index
007 Pediatrics and Pediatric Surgery
022 Human Genetics
025 Hematology
030 Pharmacology
LANGUAGE: English

AB The material consisted of all patients with a firm or highly probable diagnosis of **von Willebrand**'s disease and seen at the coagulation laboratories in Malmo, Stockholm or Gothenburg in the years 1956-1967. Inquiries were made into all of the families of the patients included in the investigation. When possible, laboratory studies were made of the closest relatives of the probands, particularly their parents, siblings and children. The material presumably includes all known cases of **von Willebrand**'s disease in Sweden up to the end of 1967. The diagnosis requires special laboratory facilities, at present available only in Malmo, Stockholm and Gothenburg. The investigation included a careful inquiry into the probands' history regarding bleeding symptoms and the information obtained was, as a rule, supplemented by data from earlier hospital records in those cases in which the patients had sought medical advice or had been admitted to hospital because of their hemorrhagic symptoms. In most cases, and particularly in probands, a complete investigation was made of the patient's bleeding and coagulation status. Examination of relatives of the probands was often limited to determinations of the bleeding time according to Duke and Ivy and of the antihemophilic factor (AHF). The probands were all examined several times and at least on one occasion during a period when they were not bleeding. Relatives were also often examined more than once, especially in doubtful cases. **Von Willebrand**'s disease is characterised by low AHF activity in the plasma and a prolonged bleeding time. These criteria together with reduced platelet adhesiveness have hitherto constituted the diagnostic criteria for **von Willebrand**'s disease. Typical of the disease is also the response to infusion of factor VIII concentrate (**Fraction** I O, **cryoprecipitate**). Infusion of such concentrates in patients with **von Willebrand**'s disease normalizes the bleeding time and often produces a retarded increase in AHF activity in the plasma. Some of the Swedish patients with **von Willebrand**'s disease presented in this study were examined immunologically for AHF related antigen. 23 families from the Swedish series of **von Willebrand**'s disease were examined with the immunological method. It was found that 51 patients belong to 15 families had a low content of AHF related antigenic material. All affected members of these families had low values, while unaffected members had normal values. However, 19 patients belonging to 8 families had normal values of AHF related protein. In families belonging to type 1 the mode of inheritance was well compatible with autosomal dominant heredity. In the 8 families with **von Willebrand**'s disease of type 2, i.e. with a normal content of AHF related protein, none of the affected males had affected sons, and of the members studied, none of the affected men studied had healthy daughters. The mode of inheritance in these families is obviously X chromosomal. As a rule, the male members had symptoms more often than

the females, in whom the disease was discovered in family studies of members who had often had no symptoms. They were thus sometimes only carriers of the disease. It would thus appear as if **von Willebrand**'s disease, which has hitherto been regarded as a single clinical entity with a unique molecular pathology, is in reality 2 separate diseases. Type 1 corresponds to the classical type of **von Willebrand**'s disease with prolonged Duke bleeding time in severe cases and, as a rule, with low platelet adhesiveness according to Salzman. Severe cases with prolonged Duke bleeding time also occur in type 2 but, as a rule, the Duke bleeding time is normal and only the Ivy bleeding time prolonged. Further, adhesiveness according to Salzmann is often normal. It appears that **von Willebrand**'s disease, type 2, is a separate disease with a clinical picture closely resembling that of the classical type of **von Willebrand**'s disease, but with certain features resembling those of mild hemophilia A, especially regarding its mode of inheritance. Occasional families with similar characteristics have been described previously.

L69 ANSWER 6 OF 6 MEDLINE on STN
ACCESSION NUMBER: 66046500 MEDLINE
DOCUMENT NUMBER: PubMed ID: 5846510
TITLE: Clinical use of a new **glycine-precipitated** antihemophilic **fraction.**
AUTHOR: Webster W P; Roberts H R; Thelin G M; Wagner R H; Brinkhous K M
SOURCE: American journal of the medical sciences, (1965 Dec) 250 (6) 643-51.
Journal code: 0370506. ISSN: 0002-9629.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 196602
ENTRY DATE: Entered STN: 19900101
Last Updated on STN: 19990129
Entered Medline: 19660211

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=> d que stat l73
L54             1 SEA FILE=REGISTRY ABB=ON  9001-27-8/RN
L55             1 SEA FILE=REGISTRY ABB=ON  109319-16-6/RN
L56             1 SEA FILE=REGISTRY ABB=ON  56-40-6/RN
L57             1 SEA FILE=REGISTRY ABB=ON  7647-14-5/RN
L58         10492 SEA FILE=HCAPLUS ABB=ON  (L54 OR ?FACTOR?(W)VIIIC) OR (L55 OR
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L61             6 SEA FILE=HCAPLUS ABB=ON  L59 AND (L57 OR NACL OR ?SODIUM?(W)?CH
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L63             2 SEA FILE=HCAPLUS ABB=ON  L62 AND (?AMINO?(W)?ACID? OR (?ALKALI?
                   OR ?ALKALINE?)(W)?METAL?)
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L65            15 SEA FILE=HCAPLUS ABB=ON  L62 OR L63 OR L64
L66             2 SEA FILE=HCAPLUS ABB=ON  L65 AND (?STABILIZ? OR ?PASTEURIZ?)
L70           277 SEA FILE=USPATFULL ABB=ON  L65 OR L66
L71           241 SEA FILE=USPATFULL ABB=ON  L70 AND (PRD<20021001 OR PD<20021001
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L72           154 SEA FILE=USPATFULL ABB=ON  L71 AND ((L57 OR NACL OR ?SODIUM?(W)
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L73             7 SEA FILE=USPATFULL ABB=ON  L72 AND ?FRACTIONAL?(W)(?PRECIPITAT?
                   OR ?CONCENTRAT?)

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L73  ANSWER 1 OF 7  USPATFULL on STN
ACCESSION NUMBER:        2003:134595  USPATFULL
TITLE:                   Compositions and methods for treating hemorrhagic virus
                         infections and other disorders
INVENTOR(S):             Fredeking, Terry M., Bedford, TX, UNITED STATES
                         Ignatyev, George M., Koltsovo, RUSSIAN FEDERATION

                              NUMBER         KIND    DATE
                         --------------- ------ --------
PATENT INFORMATION:      US 2003092684      A1   20030515
APPLICATION INFO.:       US 2002-38557      A1   20020103  (10)
RELATED APPLN. INFO.:    Division of Ser. No. US 2001-840707, filed on 23 Apr
                         2001, PENDING Division of Ser. No. US 2000-562979,
                         filed on 27 Apr 2000, PENDING

                                NUMBER         DATE
                         ------------------ --------
PRIORITY INFORMATION:    US 1999-198210P    19990427 (60)          <--
DOCUMENT TYPE:           Utility
FILE SEGMENT:            APPLICATION
LEGAL REPRESENTATIVE:    HELLER EHRMAN WHITE & MCAULIFFE LLP, 4250 EXECUTIVE SQ,
                         7TH FLOOR, LA JOLLA, CA, 92037
NUMBER OF CLAIMS:        7
EXEMPLARY CLAIM:         1
LINE COUNT:              5807
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB       Methods for the treatment or prevention of disorders, including acute
         inflammatory disorders involving pathological responses of the immune
         system, such as viral hemorrhagic diseases, sepsis, rheumatoid arthritis
         and other autoimmune disorders, acute cardiovascular events, flare-ups
         and acute phases of multiple sclerosis, wasting disorders and other
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disorders involving deleterious expression of cytokines and other factors, are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 2 OF 7 USPATFULL on STN

ACCESSION NUMBER:	2002:149120 USPATFULL			
TITLE:	Compositions and methods for treating hemorrhagic virus infections and other disorders			
INVENTOR(S):	Fredeking, Terry M., Bedford, TX, UNITED STATES Ignatyev, George M., Koltsovo, RUSSIAN FEDERATION			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2002077276	A1	20020620	<--
APPLICATION INFO.:	US 2001-840707	A1	20010423 (9)	
RELATED APPLN. INFO.:	Division of Ser. No. US 2000-562979, filed on 27 Apr 2000, PENDING			
	NUMBER		DATE	
PRIORITY INFORMATION:	US 1999-198210P		19990427 (60)	<--
DOCUMENT TYPE:	Utility			
FILE SEGMENT:	APPLICATION			
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 4250 EXECUTIVE SQ, 7TH FLOOR, LA JOLLA, CA, 92037			
NUMBER OF CLAIMS:	45			
EXEMPLARY CLAIM:	1			
LINE COUNT:	5911			

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Cytokine-receptor and cytokine antagonist-enriched blood-dervided compositions and methods of preparing and using the compositions are provided. Also provided are compositions and methods for the treatment or prevention of disorders, especially acute inflammatory disorders involving pathological responses of the immune system, such as viral hemorrhagic diseases, sepsis, rheumatoid arthritis and other autoimmune disorders, acute cardiovascular events, flare-ups and acute phases of multiple sclerosis, wasting disorders and other disorders involving deleterious expression of cytokines and other factors, including tumor necrosis factor (TNF) and interleukin-1 (IL-1) are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 3 OF 7 USPATFULL on STN

ACCESSION NUMBER:	2000:153262 USPATFULL			
TITLE:	Defined enzyme mixtures for obtaining cells and treating wounds			
INVENTOR(S):	Markert, Claus Otto, Schifferstadt, Germany, Federal Republic of Thom, Hans, Limburgerhof, Germany, Federal Republic of Weymann, Jurgen, Bad Durkheim, Germany, Federal Republic of Zahn, Wolfgang, Altrip, Germany, Federal Republic of			
PATENT ASSIGNEE(S):	Knoll Aktiengesellschaft, Ludwigshafen, Germany, Federal Republic of (non-U.S. corporation)			
	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 6146626		20001114	<--

	WO 9628543	19960919	<--
APPLICATION INFO.:	US 1997-913396	19970916	(8)
	WO 1996-EP1044	19960312	
		19970916	PCT 371 date
		19970916	PCT 102(e) date

	NUMBER	DATE	
PRIORITY INFORMATION:	DE 1995-19509584	19950316	<--
	DE 1995-19532906	19950907	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Lilling, Herbert J.
LEGAL REPRESENTATIVE: Keil & Weinkauf
NUMBER OF CLAIMS: 5
EXEMPLARY CLAIM: 1
LINE COUNT: 836
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to the use of mixtures of defined composition of purified enzymes from Clostridium histolyticum for obtaining, in a reproducible, standardized manner, cells or tissue fragments from human or animal tissues, and to these enzymes and mixtures thereof; in addition it relates to the direct or indirect medical use of these enzymes, alone or as ingredient of mixtures, eg. in wound treatment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 4 OF 7 USPATFULL on STN
ACCESSION NUMBER: 84:4558 USPATFULL
TITLE: Enriched plasma derivative for enhancement of wound closure and coverage
INVENTOR(S): Stroetmann, Michael, Munster, Germany, Federal Republic of
PATENT ASSIGNEE(S): Serapharm Michael Stroetmann, Munster, Germany, Federal Republic of (non-U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 4427651		19840124	<--
APPLICATION INFO.:	US 1982-385665		19820607	(6)

	NUMBER	DATE	
PRIORITY INFORMATION:	DE 1981-3124962	19810625	<--

DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Rosen, Sam
LEGAL REPRESENTATIVE: Hueschen, Gordon W.
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
LINE COUNT: 600
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A sprayable preparation for accelerated hemostasis and optimized biochemical control of wound closure contains a powdery mixture of 15 to 60% by weight of thrombin, 5 to 80% by weight of a desiccating and **stabilizing** agent, viz., albumin, globulin and/or fibrinogen, and 1 to 10% by weight of a fibrinolysis inhibitor. The powdery mixture is suspended in a low-boiling, anhydrous solvent, which is used as a propellant. For effective wound closure and coverage, a spray jet of

this suspension is directed onto the wound under evaporation of the solvent so that substantially only the dry, solid powdery mixture reaches the wound. This method of application by spraying is also disclosed.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 5 OF 7 USPATFULL on STN

ACCESSION NUMBER:	84:4557 USPATFULL			
TITLE:	Enriched plasma derivative for advancement of wound closure and healing			
INVENTOR(S):	Stroetmann, Michael, Munster, Germany, Federal Republic of			
PATENT ASSIGNEE(S):	Serapharm Michael Stroetmann, Munster, Germany, Federal Republic of (non-U.S. corporation)			

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 4427650		19840124		<--
APPLICATION INFO.:	US 1982-385664		19820607	(6)	

	NUMBER	DATE	
PRIORITY INFORMATION:	DE 1981-3124962	19810625	<--
	EP 1981-110615	19811218	<--

DOCUMENT TYPE:	Utility
FILE SEGMENT:	Granted
PRIMARY EXAMINER:	Rosen, Sam
LEGAL REPRESENTATIVE:	Hueschen, Gordon W.
NUMBER OF CLAIMS:	13
EXEMPLARY CLAIM:	1
LINE COUNT:	580

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A preparation for accelerated hemostasis and optimized biochemical control of wound closure ("tissue adhesive") consists only of solid, powdery, biologically active constituents and contains 60 to 96% by weight of fibrinogen, which is largely liberated from cryo-insoluble globulin, 0.05 to 5% by weight of a fibrinolysis inhibitor, and 0.1 to 15% by weight of thrombin and/or prothrombin. For use, this enriched plasma derivative may be applied in the form of a dry, powdery mixture immediately and directly onto the wound or in the area of operation, respectively. Further application methods provide atomizing, spraying, or foaming of the powdery mixture by means of a propellant.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 6 OF 7 USPATFULL on STN

ACCESSION NUMBER:	78:8611 USPATFULL			
TITLE:	Blood fractionation process using block copolymers of ethylene oxide and polyoxypropylene			
INVENTOR(S):	Kehm, Walter C., Scarsdale, NY, United States			
PATENT ASSIGNEE(S):	Baxter Travenol Laboratories, Inc., Deerfield, IL, United States (U.S. corporation)			

	NUMBER	KIND	DATE		
PATENT INFORMATION:	US 4073886		19780214		<--
APPLICATION INFO.:	US 1973-327892		19730130	(5)	

DOCUMENT TYPE:	Utility

FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
LEGAL REPRESENTATIVE: Flattery, Paul C., Flynn, Lawrence W., Hensley, Max D.
NUMBER OF CLAIMS: 7
EXEMPLARY CLAIM: 1
LINE COUNT: 412
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of separating proteinaceous and lipid materials from blood serum and plasma which comprises selective precipitation with block copolymers of ethylene oxide and polyoxypropylene polymer.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L73 ANSWER 7 OF 7 USPATFULL on STN
ACCESSION NUMBER: 76:26117 USPATFULL
TITLE: Fractionation of blood using block copolymer of ethylene oxide and polyoxypropylene polymer to recover fraction suitable for organ perfusate
INVENTOR(S): Garcia, Luis A., Huntington Beach, CA, United States
Ordonez, Guido A., Laguna Beach, CA, United States
PATENT ASSIGNEE(S): Baxter Laboratories, Inc., Deerfield, IL, United States (U.S. corporation)

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 3956259		19760511	<--
APPLICATION INFO.:	US 1974-476961		19740606 (5)	

RELATED APPLN. INFO.: Division of Ser. No. US 1973-327893, filed on 30 Jan 1973
DOCUMENT TYPE: Utility
FILE SEGMENT: Granted
PRIMARY EXAMINER: Schain, Howard E.
LEGAL REPRESENTATIVE: Altman, Louis, Flynn, Lawrence W., Hensley, Max D.
NUMBER OF CLAIMS: 2
EXEMPLARY CLAIM: 1
LINE COUNT: 359
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method of fractionating coagulation factor-depleted blood serum or plasma by selective precipitation with block copolymers of ethylene oxide and polyoxypropylene polymer to provide immunoglobulin preparations, albumin-containing fractions and organ perfusates.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.